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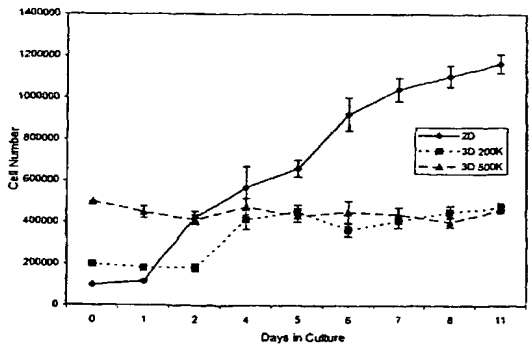
(54) Title: MODULATION OF CELL INTRINSIC STRAIN TO CONTROL MATRIX SYNTHESIS, SECRETION, ORGANIZATION AND REMODELING



Growth curves for avian internal fibroblasts grown in 2-D polystyrene culture dishes covalently bonded with type I collagen and BATs plated at 200K or 500K cells in collagen gels in Tissue Train culture plates. Cells in 2-D cultures entered log phase and passed through several division cycles whereas cells in 3-D gels plated at 200K cells per gel divided once and those plated at 500K cells per gel did not divide.

(57) Abstract: The present invention provides methods for manipulating the intrinsic strain of cells by treating tissue engineered constructs or native tissue with compounds which affect the intrinsic strain setpoint of the cells in order to modulate matrix synthesis, secretion, organization and/or remodeling so that the tissues withstand in vivo mechanical forces and have the structural characteristics of host tissue which has been permanently altered by injury, atrophy or disease. The compounds include binding site peptides, ATP, UTP and related analogues, IL-1&bgr;, TGF-&agr;, cytochalasin D, hyaluronic acid, nocodazole and others. Also provided are methods for applying a mechanical external strain to the tissues, as well as methods for modulating the expression of cytoskeletal genes that transcribe cytoskeletal proteins which regulate a cell's intrinsic strain setpoint.

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